16-20, and 22-26 stand rejected for anticipation by Ferrer Internacional, S.A. (International Publication No. WO 01/72288; hereafter "Ferrer"). Claim 15 is free of the prior art. Applicants traverse these rejections.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-3, 5, 7-20, and 22-26 stand rejected for lack of enablement. The basis for the rejection is the Office's belief that "the scope is excessive in view of the disclosed enabling exemplifications." The Examiner also states that "Applicant than [sic] complains that the instant Office action appears to have ignored the Wands factors." This rejection is respectfully traversed. As an initial matter, Applicants for the record note that they did not state that the Office ignored the *Wands* analysis, but rather that the Office appears to have refused to consider Applicants' *Wands* analysis in full.

According to the Examiner, there are two, separate enablement rejections. The first of these rejections simply concludes that the scope of the claims is excessive in view of the disclosure; the second of these rejections concludes that the scope of the claims is excessive after a purported *Wands* analysis. Since *In re Wands* is the controlling law on enablement, Applicants again address the rejection based on the *Wands* factors. Applicants also note that consideration of the *Wands* factors requires findings of fact, and enablement is determined based on a consideration of the facts as a whole (see. M.P.E.P. § 2164.01(a)).

(A) Breadth of the Claims.

In considering this first factor, the Office merely concludes that the scope is excessive because the claims recite generic terms. As noted above, a *Wands* analysis requires findings of fact. Here the Examiner has made no factual finding other than noting that the claims are generic. While the claims are generic, Applicants have provided exemplary embodiments of the individual conditions, numerous compounds to achieve the claimed effects, exemplary doses, formulations, and routes of administration of these compounds, exemplary patient populations, sound scientific argument to support the effectiveness of the claimed compounds for the full scope as claimed and methods of assessing therapeutic efficacy, with the prior art providing additional information on the bioavailability of these compounds. Therefore, Applicants have provided disclosure that bears a reasonable correlation to the scope of the claims.

(B) Nature of the Invention.

The Office has now correctly noted that the claims are directed to treatment of sleep or sleep-related disorders.

(C) The State of the Prior Art.

In characterizing the prior art, the Office states that "CDP-choline is associated in some prior art references with the effective amelioration of insomnia." Applicants have previously emphasized that the individuals treated with CDP-choline in the prior art suffered from cerebral injuries. Applicants also note that at one time the Office rejected the instant claims as being anticipated by no fewer than six references. While Applicants

have distinguished each of these cited references from the instant claims, the cited art is relevant to conditions related to, yet distinct from, those instantly claimed and therefore provides guidance to one skilled in the art, when combined with the instant disclosure.

(D) The Level of One of Ordinary Skill.

The Examiner has again misconstrued this prong of the analysis as relating to what is known in the prior art about the effects of the claimed compounds on the claimed conditions. On this point, the Examiner has also stated: Applicant alleges that the level of skill of the ordinary practitioner is directly correlated with the level of education of said practitioner. Examiner disagrees, because even the most highly educated practitioner would be unable to practice the instant claimed methods…"

Applicants again assert that the level of one of ordinary skill in this art is that of a Ph.D. level medicinal chemist or a medical doctor and that determination of the level of skill has nothing to do with what is known in the prior art about administration of CDP-choline. Applicants also assert that, at least in the pharmaceutical arts, the education level of the skilled practitioner does directly correlate with skill. Accordingly, these individuals have a high level of skill in the pharmaceutical arts. Such individuals would be able to practice the claimed methods based on the present disclosure. As discussed above, Applicants have provided exemplary embodiments of the individual conditions, numerous compounds to achieve the claimed effects, exemplary doses, formulations, and routes of administration of these compounds, exemplary patient populations, sound scientific argument to support the effectiveness of the claimed compounds for the full

scope as claimed and methods of assessing therapeutic efficacy, because optimization of these parameters, once provided by Applicants, is routine in the art. Finally, Applicants note that the Examiner has responded to a discussion of facts with a simple conclusion that no one could practice the instant methods.

(E) The Level of Predictability in the Art.

With respect to this prong, the Examiner merely states that the art of treating sleep disorders in highly variable in its predictability because of the large array of different causes or circumstances under which it is observed to occur. This view is again undermined by the six references that have been cited by the Examiner during prosecution of this application. As discussed above, Applicants' specification includes experimental data and scientific reasoning to support the effectiveness of the claimed compounds for the full scope as claimed. Furthermore, six references that discuss conditions related to those instantly claimed have been cited in this application.

(F) The Amount of Direction Provided by the Inventor.

Here again, the Office has only considered the experimental data provided by the Applicants. In addition to these data, Applicants provide lists of specific compounds for use in the methods of the invention, preferred dosages, formulations, and routes of administration of these compounds, exemplary patient populations, sound scientific argument to support the effectiveness of the claimed compounds for the full scope as claimed, and methods of assessing therapeutic efficacy. Given this disclosure and the prior art, nothing more is required to allow the skilled artisan to practice the invention.

(G) The Existence of Working Examples.

In commenting on this factor, the Office acknowledges that Applicants have provided a working example but is unable to discern the conditions being treated. As is stated in the specification on page 7, Figure 1 shows data indicating the CDP-choline improves sleep quality, Figures 2A-2B show the normalization of the sleep/wake cycle of a cocaine user after administration of CDP-choline. As Applicants have provided a working example, the Examiner must "evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims." The Examiner continues to fail to do so. Moreover, Applicants provide scientific reasoning in the specification to support the effectiveness of the claimed compounds for the full scope as claimed.

(H) The Quantity of Experimentation Needed to Make or Use the Invention Based on the Content of the Disclosure.

For this prong, the Examiner concludes that the quantity of experimentation is excessive "in light of the indefiniteness and functionality of the claims." Again, the Examiner has failed to make any findings of fact to support this conclusion. The Examiner has also only considered the experimental data provided and not the scientific reasoning or exemplary conditions, compounds, dosages, formulations, routes of administration, patient populations, and assay methods provided. As is discussed below, the instant claims, though generic, are definite because one skilled in the art would understand their metes and bounds. Furthermore, indefiniteness is not a basis for an

enablement rejection. The Office's reference to functionality is unclear, and Applicants have no found no support that functional language in claims forms the basis of an enablement rejection.

In the pharmaceutical arts, experimentation to determine the optimum chemical composition, formulation, and dosage for treating a particular condition is routine once the lead compounds are identified. In the present case, Applicants have provided exemplary assays for determining the effectiveness of various compounds, a defined list of specific compounds, preferred dosages, formulations, and patient populations. Accordingly, Applicants have provided a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

A consideration of the *Wands* factors indicates that the instant claims are enabled. Reconsideration of this rejection is requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 12-15, 17, 19, 22, 27, and 28 stand rejected for indefiniteness. Claims 27 and 28 are no longer pending.

The purpose of the definiteness requirement is to ensure that "the scope of the claim is clear to a hypothetical person possessing the ordinary skill in the pertinent art" (M.P.E.P. § 2171). Furthermore, M.P.E.P. § 2173.02 states:

> Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
> (A) The content of the particular application disclosure;
> (B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

In addition, "[b]readth of a claim is not to be equated with indefiniteness" (M.P.E.P. § 2173.04). The instant claims are definite under this standard. Each of the bases for rejection will be addressed in turn.

With respect to the rejections of claims 1, 12, 15, 17, and 22 for reciting "compound comprising," the Office states that the term "comprising" implies "that the compounds listed in the claims following the term 'compound comprising' are by implication not the only compounds being claims," in response to Applicants' previous arguments. Applicants agree with the Examiner's conclusion that the claim is not limited to administration of the specific molecular species recited in the claim.

To further clarify the rejection, the Examiner states that the rejection "is in effect asking for well defined metes and bounds for the set of claimed active ingredients." Again, there is no legal requirement for "well defined metes and bounds." Instead, the standard is whether the skilled artisan can determine the scope of the claim. Furthermore, M.P.E.P. § 2173.05(t) states, "Chemical compounds may be claimed by a name that adequately describes the material to one skilled in the art." Thus, as previously argued, as classes are routinely used to refer to numerous related compounds both in the scientific and the patent literature, Applicants again assert that one skilled in the art would understand the scope of "a compound comprising cytidine, cytidine monophosphate (CMP)..." as recited in the instant claims. In reply to these arguments, the Office has not

provided any evidence or reasoning why one skilled in the art is not apprised of the scope of the claims.

For this rejection, the Examiner further asserts that "applicant is not being unfairly denied the breadth of the claimed subject matter necessary to exclude infringers" and suggests changing the wording of the claim to recite "compound consisting of" instead of "compound comprising." Applicants decline to accept this suggestion as it would limit the scope of the claim to certain preferred embodiments that are not commensurate with the breadth of the invention. Applicants again request reconsideration and withdrawal of the rejection.

With respect to the rejection of claims 12, 13, 19, and 23, the rejection appears to be based on a desire by the Examiner to have the Applicants list every possible existing physical condition (for claim 12) and substance abuse disorder (for claims 13, 19, and 23) in the claim, whether positively or negatively recited. Applicants base this conclusion on comments by the Examiner that for claim 12 "the particular 'existing physical limitation[s]" have not been specified in the claim" and for claims 13, 19, and 23 "the particular 'substance abuse disorder' has not been specified." In reply, Applicants have repeatedly noted that generic terms such as "existing physical condition" and "substance abuse disorder" are not indefinite because they do not list "particular" disorders or conditions. Applicants have also provided evidence that these generic terms are known in the art via PubMed searches of the term "physical condition" yielding 1195 references and of the term "substance abuse disorder" yielding 60 references. The Examiner has

never stated why one skilled in the art would not understand the metes and bounds of these claims. Accordingly, the rejection cannot stand.

With respect to the dependency of claim 13 from claim 12 and claim 23 from claim 22, the Examiner states, "Applicant appears to be arguing that 'caused by substance abuse' is somehow hidden within the terms that define claim 12 [and 22]." The Examiner is correct in the sense that claims 12 and 22 are directed to sleep disorders in general (with certain provisos), and claims 13 and 23 are directed to a subset of sleep disorders, i.e., those caused by a substance abuse disorder, consistent with 35 U.S.C. § 112, fourth paragraph. Applicants also again point out that claims 13 and 23 recite the indefinite article "a" and not the definite article "the" with respect to substance abuse disorder. Applicants have reviewed M.P.E.P. § 2173.05(e) where all examples of improper antecedent basis involve use of "said" or "the," i.e., definite articles, and not "a." The claims are correctly drafted, and the rejection should be withdrawn.

Finally, the Examiner has rejected claims 1, 12, 17, and 22 because in his view "the claims appears [sic] to be self-contradictory." The basis of this rejection appears to be that the Examiner has equated insomnia with an abnormal sleep/wake cycle. This position of the Examiner ignores the fact that abnormal sleep/wake cycles may be the result of sleeping too much, rather than sleeping too little. Accordingly, there is no contradiction in claiming a method of normalizing the sleep/wake cycle and not treating insomnia.

None of the other independent claims recite "sleep/wake cycle." Claims 12 and 22 recite a method for treating a sleep disorder, and the Examiner has provided no reason why all sleep disorders must include insomnia. Indeed, narcolepsy often involves falling asleep at inappropriate times during the day. Furthermore, claim 17 recites a method of increasing cognitive function in a sleep-deprived mammal, and the Examiner has again provided no reason why a sleep-deprived mammal, e.g., a student staying up late to study for an exam, must have insomnia. Applicants submit that there is no contradiction between the preambles of claims 12, 17, and 22 and an exclusion of insomnia.

This final rejection under 35 U.S.C. § 112, second paragraph may also be withdrawn.

Obviousness-type Double Patenting

Claims 1-3, 5, and 7-29 stand rejected for obviousness-type double patenting over claims 1-16 of Renshaw (U.S. Patent No. 6,103,703) for "substantially overlapping subject matter." Claims 27-29 have been cancelled. The standard for obviousness-type double patenting is "does any claim in the application define an invention that is merely an obvious variation of an invention claimed in the patent?" (M.P.E.P. § 804).

The Examiner appears to maintain the rejection based on the conclusion that "'a sleep disorder' is properly included within the metes and bounds of the term 'stimulant-induced disorder'" and that this inclusion proves obviousness. Applicants disagree as a

species is not necessarily rendered obvious by a genus encompassing it. On this point, M.P.E.P. § 804 (II) states:

> Domination and double patenting should not be confused. They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim which fully encompasses or reads on an invention defined in a narrower or more specific claim in another patent or application. *Domination by itself*, i.e., in the absence of statutory or nonstatutory double patenting grounds, *cannot support a double patenting rejection.* (Emphasis added)

Based on this standard, domination of the present claims by the generic claims of Renshaw cannot be the sole basis of a double patenting rejection. As the Examiner has advanced no other reason, the rejection must be withdrawn.

In addition, Applicants again point out that not all of the present claims are directed to methods of treating a sleep disorder. Accordingly, even if the Examiner had applied the correct legal standard, he has failed to support the rejection with respect to claims 1 and 17, which do not recite the term "sleep disorder."

The Examiner also states that Applicants argued that Renshaw "fails to further include the step of administering 'a cytidine-containing compound' … or in particular 'CDP-choline'…" Applicants did not make such an argument, and the basis for the Examiner's assertion is unclear. For the record, Applicants actually stated: "there is nothing in the claims of Renshaw that would indicate that a cytidine-containing compound would treat a sleep disorder as instantly claimed." Furthermore, Applicants have never used the term "CDP-choline" in arguments with respect to the double-patenting rejection.

The rejection should be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-3, 5, 7-14, and 16-20 stand rejected for anticipation by Fernandez; claims 1-3, 5, 7-14, 16-20, and 22-26 stand rejected for anticipation by Ferrer; and claims 17, 18, and 20 stand rejected for anticipation by Wurtman. In order to anticipate a claim, a prior art reference must teach each and every limitation. Applicants again traverse these rejections.

Fernandez

The basis for the rejection of all independent claims over Fernandez is that "the administration of CDP-choline to treat insomnia is specifically taught." The Examiner has maintained the rejection because he equates an abnormal sleep/wake cycle with insomnia and further believes that the preambles of the present claims have been in effect deleted. For the reasons stated above in response to the indefiniteness rejections, exclusion of insomnia from methods of normalizing the sleep/wake cycle, treating a sleep disorder, and increasing cognitive function in a sleep deprived mammal does not in effect delete the preamble. As all of the independent claims exclude treatment of insomnia, this rejection remains moot.

Wurtman

The Office has maintained the rejection of claims 17, 18, and 20 over Wurtman for a variety of reasons, none of which addresses Applicants' arguments. In particular, claim 20 does not depend from claim 17. As previously argued, Applicants have not claimed increasing cognitive function under any circumstance. Claim 17, directed to increasing cognitive function in a sleep deprived mammal, is not anticipated by Wurtman because the reference fails to teach administration of the compound to mammals **deprived of sleep** in order to increase cognitive function. Without such a teaching, Wurtman cannot anticipate the claims because it does not disclose, either expressly or inherently, each and every limitation of claim 17.

Ferrer

The basis for the rejection over Ferrer is that "applicant has not excluded 'disorientation' and other symptoms." The relevance of this basis is unclear. The present claims are directed to methods of normalizing the sleep/wake cycle; treating sleep disorder; and increasing cognitive function in a sleep-deprived mammal. As the Office has not alleged that Ferrer teaches any of these methods, this final § 102 rejection should also be withdrawn.

CONCLUSION

Applicants submit that claims are in condition for allowance, and such action is respectfully requested. Enclosed is a Petition to extend the period for replying for three months, to and including February 7, 2008. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: February 7, 2008

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